Eukaryotic expression systems for testing the properties of tick-borne encephalitis virus proteins.

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Tick-borne encephalitis virus (TBEV) is a ssRNA zoonotic flavivirus belonging to the *Flaviviridae* family. To the best of our knowledge, three TBEV subtypes have been identified so far: European (TBEV-Eur), Far Eastern (TBEV-FE) and Siberian (TBEV-Sib). In natural habitat TBEV is maintained by two species of ticks from the *Ixodes* genus: *I. ricinus* transmitting TBEV-Eur and *I. persulcatus*, the main vector for TBEV-Sib and TBEV-FE.

In humans, TBEV causes tick-borne encephalitis (TBE), a severe neurological disease which may lead to serious medical complications, including meningitis and meningoencephalitis. Approximately 10 000–12 000 clinical cases of tick-borne encephalitis reported each year, make TBEV one of the most medically important arthropod vector transmitted virus (arbovirus) in eastern, central and northern Europe, northern China, Japan and Mongolia, and the Russian Federation. Currently, there are four vaccines against TBEV available in the market; two manufactured in Europe based on inactivated TBEV-Eur strains and two manufactured in the Russian Federation based on inactivated TBEV-FE strains. Vaccinations are not mandatory but recommended only for residents and tourists traveling in endemic areas. However, no specific antiviral drug therapy is available for people already infected with TBEV and the only accessible form of TBE treatment is symptomatic. Symptoms like meningitis, encephalitis, or meningoencephalitis requires hospitalization and can result in long-term neurological afflictions or even death. Severity of TBE disease implications and the increasing population of ticks incline towards the development of efficient antiviral therapy against TBEV.

Considering that TBEV is a BSL-3 class pathogen, the main aim of my research is construction of various tools for testing the antiviral activity of potential drugs without the risk of exposer to the virus and necessity of working in a BSL-3 cabinet. For that purpose, using retroviral delivery system I have constructed cell lines stably expressing two of TBEV proteins: protein prM and glycoprotein E, which enable the production of virus-like particles. Since glycosylation of E protein shows high importance in the process of viral entry as well as production of viral particles, inhibitors targeting the glycosylation process present a lot of promise in search of potential drugs. Experiments with glycosylation inhibitor tunicamycin showed, that stable cell lines expressing TBEV proteins might be useful in further investigation of potential antiviral compounds. Expression of protein prM and glycoprotein E was also obtained in different expression systems: insect cell expression system

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NATIONAL COHESION STRATEGY
EUROPEAN UNION
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SOCIAL FUND

Project co-funded by European Union under the European Social Fund

derived from *Spodoptera frugiperda* and protozoan *Leishmania tarentolae* based protein expression system.